Remarks

Claims 1-6, 9-12, and 14-21 are pending in this Application. Claims 1-6, 9-12, and 14-21 stand rejected on arguments laid out in the Office Action mailed December 7, 2007.

In the present Amendment, claims 6 and 11 have been amended to remove inadvertent duplications of certain agents in the group. Claims 14-17 are canceled by the present Amendment.

Therefore, Applicant submits that no new matter is added by these amendments.

Claim objections

Claims 6 and 11 were objected to because of the informalities of certain agents being recited more than once within the same group. Applicant has amended claims 6 and 11 to remove to the inadvertent duplications of certain agents in the group.

Claim rejections – 35 USC § 112

Claims 1-6, 9-12, and 14-21 stand rejected under the first paragraph of 35 U.S.C. § 112 for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite chlorotoxin derivatives comprising certain sequences. In laying out the grounds for this rejection, the Examiner argues that there are many different peptides within the genus claimed and that the specification is not enabling for so many different peptides. The Examiner calculates that from SEQ ID NO: 13 alone, there are well over 4800 different 9 amino-acid peptides possible.

Applicant respectfully submits that the relevant analysis is not related to the possible number of peptides encompassed by the claims. Rather, the relevant analysis is whether those of ordinary skill in the art would recognize the inventor to have been in possession of the claimed invention at the time of filing. Indeed, description of an infinite number of peptides is possible so long as the specification combined with general knowledge in the art provides adequate guidance. See, for example, Example 5 of the Written Description Training Manual (revised March 25, 2008). In claim 1 of Example 5 of the training manual, a protein *comprising* a protein

that includes a particular amino acid sequence is recited. This claim reads on a limitless number of species because of the broad "comprising" language. Nevertheless, in Example 5, the specification was found to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, with respect to that claim because it disclosed a partial structure, relevant identifying characteristics of the claimed protein, and methods and examples of isolating the claimed protein.

Similarly, the specification of the present application discloses a partial structure, relevant identifying characteristics, and methods of making and examples of the chlorotoxin derivatives recited in the claims. Partial structures are defined in the claims according to listed sequences. Relevant identifying characteristics of the claim term "chlorotoxin derivative" are described in lines 25-32 of page 10 of the specification as originally filed. Methods of making such chlorotoxin derivatives are described in the paragraph beginning on page 10 and ending on page 11 of the specification as originally filed, and working examples of making and using such chlorotoxin derivatives are provided (see, *e.g.*, Examples 11-15, discussed below).

The Examiner asserts that "no direction is provided as to what portions are necessary to be useful in treating cancer" and that "there is no disclosure of a correlation between function and structure of the polypeptides." In contrast to the Examiner's assertion, the specification refers to "core binding sequences" (page 10 lines 25-32) *and furthermore includes description of experimental results identifying core binding sequences*. For example, Example 11 and Figures 10-12 relate to binding activity of various 10-mers derived from chlorotoxin; Example 12 and Table 4 relate to *in vivo* activity of binding regions identified in Example 11; Example 13 and Tables 5-6 describe identification of minimal binding activity of various peptides derived from chlorotoxin; Example 14, Figure 13, and Table 7 relate to the contribution of each residue in binding portions identified in previous Examples; and Example 15, Figure 14-15, and Tables 8-10 describes a comparison between binding regions of chlorotoxin and that of related toxins. Applicant respectfully submits that these Examples relate structure (through the sequences of the peptides) to function (binding activity) and also provide ample direction as to what portions and combinations can bind cancer cells and would therefore be useful in treating cancer.

Indeed, the very sequence in SEQ ID NO. 13, which is based on results gleaned from the Examples mentioned above, provides direction. Most of the residues in the sequence are limited

to a single amino acid, as the inventors had determined that they are important for binding. Most of the remaining residues are constrained to a subset of possible amino acids; this constraint encompasses the guidance from the specification as to which amino acids at certain positions are favorable for binding to cancer cells. Only two residues in the peptide are not constrained to particular amino acids; the flexibility of the sequence at these residues reflects the recognition by the inventors that the identity of the residues at such positions is not important for binding.

In light of these arguments, Applicant respectfully requests that this rejection be withdrawn.

Claim rejections – 35 USC 102

Claims 14-17 remain rejected under 35 U.S.C. 102 (b) as being anticipated by Soroceanu *et al* (Cancer Research, November 1, 1998, Vol. 58, pages 4871-4879) and as being anticipated by Lyons *et al.* (US 6,667,156). Solely in order to simplify issues and to progress prosecution toward allowance, Applicant has canceled claims 14-17 (which relate to diagnostic methods) in order to focus the present case on therapeutic methods. Thus, these rejections are rendered moot.

Claims 1, 4-6, 9-12, and 19-20 have been rejected under 35 U.S.C. 102(e) as being anticipated by Samoylova *et al.* (US 2003/0216322) as evidenced by the Merck Manual entry for methotrexate. In laying out the grounds for this rejection, the Examiner argues that Samoylova teach peptides such as ELRGDSLP, which comprises a portion (RG) of chlorotoxin (SEQ ID NO.: 1 of the current invention), thus meeting the structural limitations of a portion of a chlorotoxin derivative as recited in claims 1, 9, and their dependents. Applicant respectfully points out that claims 1, 4-6, 9-12, and 19-20 recite not just structural limitations, but also the term "chlorotoxin derivative," which is described in lines 25-32 of page 10 of the specification as originally filed. The term "chlorotoxin derivative" is specified as referring to "derivatives, analogs, polypeptide fragments and mimetics of chlorotoxin and related peptides *which retain the same activity as chlorotoxin*." (emphases added). There is no evidence provided by Samoylova *et al.* or by the Examiner that the peptides taught by Samoylova, such as ELRGDSLP, retain the same activity as chlorotoxin.

Thus, Samoylova *et al.* cannot anticipate the claimed invention. Applicant respectfully requests removal of this rejection.

Claim rejections – 35 USC 103

Claims 1-6, 9-12, and 18-21 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Samoylova *et al.* (US 2003/0216322) and Stupp *et al.* (The Lancet v2 Sept 2001 552-560). Samoylova *et al.* teach phage-derived peptides for recognition and targeting of glial cell tumors. Stupp *et al.* teach administration of temozolomide for brain tumours and glioma.

In laying out the grounds for this rejection, the Examiner argues that "one would be motivated to substitute the chlorotoxin peptide for the phage-derived peptides particularly since Samoylova specifically teach glioma as a target and also since chlorotoxin is taught to have high-affinity specific binding to glioma cells."

Applicant respectfully disagrees. Samoylova *et al.* provides a variety of synthetic peptides, none of which are chlorotoxin derivatives. Although Samoylova *et al.* mentions a chlorotoxin peptide as having binding activity to glioma cells (paragraph [0010]), chlorotoxin peptides are included in a general description of other agents that are known to bind glioma cells. Instead of directing one toward chlorotoxin peptides for use in treating gliomas, Samoylova *et al.* then argues a need for additional markers for glioma cells, citing various problems with the known markers described in paragraph [0010].

The Examiner has not explained why one would be motivated to substitute a chlorotoxin peptide for one of the phage-derived peptides when Samoylova *et al.* provides and teaches other peptides that bind to glioma cells. One of ordinary skill in the art reading Samoylova *et al.*, either alone or in combination with Strupp *et al.*, would have no motivation to substitute a chlorotoxin peptide, when Samoylova *et al.* teaches other binding peptides with high binding affinity for glioma cells.

Thus, Samoylova *et al.* in combination with Strupp *et al.* cannot render obvious the claimed invention. Applicant respectfully requests removal of this rejection.

Double patenting

Claims 9-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 13 of co-pending Application No.

10/522,810 in view of Stupp *et al.* (The Lancet v2 Sept 2001 552-560). Applicant will address this rejection upon indication of an allowance of the presently pending claims.

Conclusion

For all of these reasons, the rejections are not applicable to the claims and the claims should be allowed. A Notice to that effect is earnestly solicited.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account Number 03-1721. Applicant would like to thank the Examiner in advance for review of this request.

Respectfully submitted,

/Brenda Herschbach Jarrell/

Dated June 9, 2008

Brenda Herschbach Jarrell, Ph.D.
Reg. No.: 39,223

CHOATE, HALL & STEWART LLP
Patent Group
Two International Place
Boston, MA 02110
Tel: 617-248-5000
Fax: 617-248-4000